REMARKS

Claims 1-49 and 53-54 were previously cancelled without prejudice. Claim 61 has been withdrawn. Applicants reserve the right to file divisional applications directed to the withdrawn subject matter. Claim 56 has been amended. Support for the amendment can be found throughout the specification, specifically at page 13, line 23 - page 14, line 18. No new matter has been added. Claims 50-52, 55-60, and 62 are currently pending.

Rejection Under 35 U.S.C. §102(e)

Claims 50-52 and 55-60 have been rejected under 35 U.S.C. §102(e) as anticipated by Tsuji *et al.* (U.S. Patent Application No. 2003/0157135; hereinafter "Tsuji"). The Examiner states that Tsuji teaches the administration of galactosylceramide to modulate the immune response in a mammal. See Office Action page 4. The Examiner also states that, because of its immunostimulatory nature, the administration of galactosylceramide would necessarily modulate the immune response in an individual regardless of the type of disease. See Office Action page 4. In response to applicants arguments filed on August 5, 2008, the Examiner contends that the composition taught by Tsuji is a mammalian metabolite. See Office Action pages 2-3.

The Examiner comments on page 3 of the Office Action "And Tsuji *et al.*, teaches both galctosylceramide and glucosylceramide." Applicants respectfully disagree with the Examiner's characterization of the reference. The Tsuji reference is more accurately described as teaching both an *α-galactosylceramide* and an *α-glucosylceramide*. This generalization of the results described in Tsuji is also evident from the Examiner's comments on page 4 of the Office Action: "Tsuji *et al.*, teaches that galactosylceramide is immunostimulatory..." As stated above, Tsuji teaches only that *α-galactosylceramide* is immunostimulatory.

Applicants respectfully note the present claims recite the administration of a *mammalian* intermediary metabolite. It is therefore irrelevant that this compound is "appreciated" as being a mammalian metabolite. The important consideration is whether the compound is in fact a mammalian intermediary metabolite. The fact that two structures are chemically similar provides an insufficient basis to assert that "...the composition of Tsuji *et al.*, is the same as those recited in the claims..." See Office Action page 3. The background section of the present

application describes the use of an α-glucosylceramide, and specifically explains that this compound is *not* a normal mammalian intermediary metabolite. The α-galactosylceramide and α-glucosylceramides utilized by Tsuji are therefore foreign to a mammalian subject. These compounds comprise an alpha linkage between a sugar moiety and a ceramide. As explained in the present specification, the alpha form of glycosylceramide has never been described in a mammal. In fact, the parent compound was originally isolated from a marine sponge. The compounds of the present invention are β-glycosylceramides which are a normal constituent of mammalian cells. Applicants respectfully assert the use of the alpha form is an essential aspect of Tsuji. In addition, Tsuji claim only structures containing an alpha linked glucosylcermaide. A clear reading of Tsuji indicates that the recited compounds are strictly limited to glycosylceramides containing an alpha linkage between the ceramide and the sugar portions.

For a rejection under 35 U.S.C. §102 to be properly made and sustained, the art cited in that rejection must disclose each and every element of the claims called out in the rejection. MPEP §2131. Tsuji does not teach the administration of a *mammalian* intermediary metabolite. Instead, Tsuji teaches the use of a non-mammalian compound. Applicants respectfully request withdrawal of the rejection of claims 50-52 and 55-60.

Rejection Under 35 U.S.C. §103(a)

Claims 50 and 62 are rejected under 35 U.S.C. §103(a) as being obvious over Tsuji. The Examiner states that although Tsuji does not teach the administration of galactocylceramide to a human, such treatment is suggested by the reference. The Examiner then concludes that it would have been *prima facie* obvious to administer galactocylceramide to a human because the immunostimulatory activity of galactocylceramide is known in the art. See Office Action pages 5-6. In response to Applicants' previously submitted arguments, the Examiner states that present claims allow for the administration of antigens, along with glycolipids such as galactosyceramide and glucosylceramide. The Examiner also states that Tsuji suggests administration to a human. See Office Action pages 5-6.

Applicants respectfully traverse the rejection and assert that claims are not obvious over Tsuji. As stated above, Tsuji neither teaches nor suggests the administration of a *mammalian*

intermediary metabolite, but rather teaches the use of a non-mammalian compound. However, solely in an effort to promote prosecution, claim 56 has been amended to recite that the monosaccharide ceramide comprises a *β-glucosylceramide* and a *β-galactosylceramide*. The presence of a β-glucosylceramide and a β-galactosylceramide in a mammalian cell has never been described in the literature. Instead, only a different variety of glucosylceramide (β-glucosylceramides) has been identified. As noted above, the present specification specifically describes the use of α-glucosylceramides and the fact that this compound is *not* a normal mammalian intermediary metabolite.

The chemical differences between beta linked glucosylceramides (which are a normal constituent of mammalian cells) and the alpha linked glucosylceramides (a chemically distinct form) would not allow for the effects of the compounds to be similar. For instance, the difference between ribonucleotides and nucleotide analogues made from arabinosylnucleosides is reflected in a transposition of the 2' hydroxyl group from one side of the ring to the other side. However, this transposition engenders a completely distinct set of properties. Furthermore, it could be expected that a foreign compound such as an alpha-linked glycosylceramide would have profound effects upon immune reactivity. One of skill in the art would have no expectation that a metabolite that is a common constituent of mammalian cells would have an immunomodulatory effect on such cells.

In addition, Tsuji teaches the use of a non-mammalian compound requiring the *co-administration* of an antigen or antigens. The Tsuji reference clearly does not recognize that a β-glycosylceramide may be used alone in the absence of an antigen. Instead, Tsuji teachs the use of α-glycosylceramides strictly as a method of augmenting the effects of an antigen. The description of the use of α-glycosylceramides as adjuvants provides no particular motivation to use the compound in the absence of antigens. The Tsuji claims recite methods: (1) utilizing antigens; (2) augmenting antigen effects; and (3) utilizing alpha glycosylceramide as an adjuvant. No claims are directed to the use of an alpha glycosylceramide alone. In addition, there are no Examples directed to the use of alpha-glucosylceramide, in the absence of antigen, with test animals. Thus, there is an absence of any teaching or suggestion in Tsuji of the therapeutic use of a β-glycosylceramde.

Tsuji does not render the present claims obvious because Tsuji requires the use of an α-glucosylceramide. In addition, one of skill in the art would have no motivation to alter the teachings of Tsuji to utilize β-glucosylceramide, nor an expectation that doing so would be successful, because the Tsuji compound (α-glucosylceramide) is not a *mammalian* intermediary metabolite as required by the present claims. As such, claims 50 and 62 are non-obvious over the Tsuji reference. Withdrawal of the rejection is respectfully requested.

Double Patenting

Claims 50-52, 55-50, and 62 are provisionally rejected in the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-6, 9, and 11 of copending U.S. Patent Application No. 10/376,906. Applicants respectfully request that the rejection be held in abeyance until the finding of allowable subject matter.

Conclusion

Applicants respectfully submit that all claims are in condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel at the number listed below to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,
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